[redacted]

STN Search History

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FILE 'HOME' ENTERED AT 12:11:07 ON 14 APR 2003
L1          822 (RESPIRATORY (A) SYNCYTIAL OR RSV) AND (F (S) (PROTEIN OR GENE
                OR POLYNULCEITDE OR CHIMER##)) (P) (G (S) (PROTEIN OR GENE OR
                POLYNULCEITDE OR CHIMER##))

L2          127 L1 AND ((RSV (5N) A AND RSV (5N) B) OR (RSV-A AND RSV-B) OR
                (VIRUS (5N) A AND VIRUS (5N) B))

L9           39 L8 AND ((RSV (5N) A AND RSV (5N) B) OR (RSV-A AND RSV-B) OR
                (VIRUS (5N) A AND VIRUS (5N) B))

 (FILE 'HOME' ENTERED AT 12:11:07 ON 14 APR 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 12:12:41 ON
     14 APR 2003
L1          822 S (RESPIRATORY (A) SYNCYTIAL OR RSV) AND (F  (S) (PROTEIN OR GE
L2          127 S L1 AND ((RSV (5N) A AND RSV (5N) B) OR (RSV-A AND RSV-B) OR (
L3           39 DUP REM L2 (88 DUPLICATES REMOVED)
L4           17 S L3 NOT PY>1995
L5           17 S L1 AND (M2-1 OR M2 ADJ ORF1 OR M2-ORF1)
L6           17 S L5 NOT L4
L7            0 S L5 NOT PY>1995
L8          163 S L1 AND (RSV (S) VACCINE)
L9           39 S L8 AND ((RSV (5N) A AND RSV (5N) B) OR (RSV-A AND RSV-B) OR
L10           9 DUP REM L9 (30 DUPLICATES REMOVED)
L11           7 S L10 NOT L4
```

L4 ANSWER 1 OF 17 MEDLINE
AN 96404055 MEDLINE
DN 96404055 PubMed ID: 8808333
TI Variation in the fusion glycoprotein gene of human **respiratory syncytial virus** subgroup **A**.
AU Plows D J; Pringle C R
CS Biological Sciences Department, University of Warwick, Coventry, UK.
SO VIRUS GENES, (1995) 11 (1) 37-45.
Journal code: 8803967. ISSN: 0920-8569.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U31558; GENBANK-U31559; GENBANK-U31560; GENBANK-U31561; GENBANK-U31562
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19980206
Entered Medline: 19961024
AB Six different genotypes (designated lineages SHL1-6) of human **respiratory syncytial** (RS) virus have been defined by partial nucleotide sequence analysis of the variable SH and the hypervariable **G** membrane **protein genes**, and by restriction fragment analysis of the conserved N **protein gene** of viruses isolated in south Birmingham. Viruses of very similar genotype appear to be present worldwide at the present time. We have determined the nucleotide sequences of the fusion protein genes of five viruses isolated in south Birmingham in the same year, but belonging to different lineages, and have compared them with the sequences of four subgroup **A viruses** isolated at earlier times from diverse localities. The sequence diversity of the **F genes** of these five viruses, as measured by nucleotide (94.5-98.5%) and inferred amino acid (97.0-99.3%) identifies, is comparable with that of the nine subgroup **A viruses** considered as a whole. No sequence changes occur in any of the sites of known epitopes. Comparison of the nine subgroup A sequences with the published sequences of a subgroup **B** strain and three bovine RS **viruses** confirms that the **F protein** sequences are most divergent in the F2 region.

L4 ANSWER 2 OF 17 MEDLINE
AN 94160508 MEDLINE
DN 94160508 PubMed ID: 8116189
TI Antigenic diversity of **respiratory syncytial** viruses and its implication for immunoprophylaxis in ruminants.
AU Duncan R B Jr; Potgieter L N
CS Department of Environmental Practice, College of Veterinary Medicine, University of Tennessee, Knoxville.
SO VETERINARY MICROBIOLOGY, (1993 Nov) 37 (3-4) 319-41. Ref: 148
Journal code: 7705469. ISSN: 0378-1135.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199403
ED Entered STN: 19940406
Last Updated on STN: 19940406
Entered Medline: 19940331

AB Bovine **respiratory syncytial** virus (BRSV) is a very important pathogen of cattle and perhaps other ruminants. It is a major contributor to the incidence of respiratory tract disease in nursing beef and feedlot and dairy calves. The genome of **respiratory syncytial** viruses encodes 10 proteins translated from 10 unique mRNAs. The major glycoprotein (**G**), fusion **protein** (**F**), 1A **protein** and the 22K **protein** are components of the viral envelope. The nucleocapsid contains the nucleocapsid protein (N), the phosphoprotein (P), and the large protein (L). The matrix protein (M) forms a structural layer between the envelope and the nucleocapsid. Antibodies to all the structural proteins develop in convalescent calves. However, evidence suggests that immunity develops primarily as a result of the antigenic stimulus by the major glycoprotein G and the fusion glycoprotein F. It is known also that activated cytotoxic T cells interact with N and **F protein** antigens and helper T cells interact with N, **F**, and 1A **protein** antigens. With the exception of the major glycoprotein, the respective proteins of various **respiratory syncytial** viruses share major antigenic domains. Based on antigenic differences of the major glycoprotein, at least 3 subgroups of **RSV** are recognized; human **A**, human **B**, and bovine **RSV**. Indirect evidence suggests that a second subgroup of BRSV exists. However, we have identified only one BRSV subgroup based on our work with RNase mismatch cleavage analysis of the **G protein gene** from a limited number of strains. Furthermore, our data indicated that **a** caprine **RSV** isolate is closely related to the bovine strains, but an ovine isolate is not. The latter may constitute yet another subgroup of **RSV**. These data affect decisions on optimization of immunoprophylaxis since evidence suggests that protection against **a** homologous **RSV** subgroup virus is superior to that against a heterologous strain in immune subjects.

L4 ANSWER 3 OF 17 MEDLINE
AN 94025890 MEDLINE
DN 94025890 PubMed ID: 8212825
TI Vaccination with a heterologous **respiratory syncytial** virus chimeric FG glycoprotein demonstrates significant subgroup cross-reactivity.
AU Oien N L; Brideau R J; Thomsen D R; Homa F L; Wathen M W
CS Cancer and Infectious Diseases Research, Upjohn Company, Kalamazoo, MI 49001.
SO VACCINE, (1993) 11 (10) 1040-8.
Journal code: 8406899. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199310
ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931029
AB A subunit vaccine candidate, termed FG, is a **chimeric** glycoprotein composed of the extracellular domains of the fusion (**F**) glycoprotein and the attachment (**G**) glycoproteins of **a** subgroup **A respiratory syncytial** virus (**RSV**). Two subgroups, **A** and **B**, of **RSV** differ primarily within the G glycoprotein. Therefore, it has been suggested that a subunit vaccine composed of the G glycoprotein would need to contain the G glycoproteins from both **RSV** subgroups. We have engineered a second **chimeric** glycoprotein, FGB, which is

composed of the **F** glycoprotein from **RSV** subgroup **A** and the **G** glycoprotein from **RSV** subgroup **B** and is expressed in baculovirus. A comparison of protection between the two subunit vaccines (FG and FGB) was performed in cotton rats after homologous and heterologous virus challenge. FG and FGB appeared to afford the same degree of protection against either homologous or heterologous challenge. Serum neutralization titres against homologous or heterologous virus were nearly equivalent following FG or FGB vaccination. Radioimmunoprecipitation using sera from rats immunized with FG or FGB revealed cross-reactivity between the two G glycoproteins. Adsorption of anti-F antibody from serum of rats immunized with FG significantly reduced the **RSV** neutralizing activity of the serum suggesting that enhanced neutralization previously observed with FG antisera compared with F antisera alone may not be entirely attributed to antibodies against the G glycoprotein but may be attributed to a function associated with the G glycoprotein portion of FG which enhances the immunogenicity of the F portion of FG.

L4 ANSWER 4 OF 17 MEDLINE
AN 93273931 MEDLINE
DN 93273931 PubMed ID: 8099086
TI Analysis of **respiratory syncytial** virus genetic variability with amplified cDNAs.
AU Sullender W M; Sun L; Anderson L J
CS Department of Pediatrics, University of Alabama, Birmingham 35233.
NC P30 AI27767 (NIAID)
P30 HD28831 (NICHD)
SO JOURNAL OF CLINICAL MICROBIOLOGY, (1993 May) 31 (5) 1224-31.
Journal code: 7505564. ISSN: 0095-1137.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930716
Last Updated on STN: 19950206
Entered Medline: 19930629
AB Antigenic and genetic heterogeneities exist within the two major antigenic groups of **respiratory syncytial** (RS) virus. We developed a polymerase chain reaction (PCR)-based assay that not only differentiates the two RS virus groups but allows distinctions within groups on the basis of changes in the nucleotide sequences, as revealed by restriction fragment analysis. In this assay, viral RNA served as a template for cDNA synthesis with extension from a synthetic oligonucleotide primer complementary to bases 164 to 186 in the **F protein** mRNA. For PCR amplification, two group-specific 5' primers were added. The two primers corresponded to the **G protein** mRNA sequence of group B (bases 10 to 30) or group **A** (bases 247 to 267) RS **virus**. Agarose gel electrophoresis readily discriminated the 1.1-kb group B and the 0.9-kb group **A virus** amplification products. All 47 viruses tested were assigned to the same group by both PCR and monoclonal antibody reaction pattern analysis. Restriction fragment analysis of the amplified DNAs revealed 12 restriction patterns for group **A viruses** and 7 restriction patterns for group **B viruses**, while the monoclonal antibody reaction patterns revealed seven patterns for group **A viruses** and 3 patterns for group **B viruses**. Most viruses with the same monoclonal antibody reaction patterns had different restriction patterns, and some viruses with the same restriction patterns had different monoclonal antibody reaction patterns. Thus, the results of the PCR assay

concurred with the monoclonal antibody reaction pattern analysis for group classification of RS viruses, while the restriction fragment analysis identified greater diversity within groups than was seen with the monoclonal antibody analysis.

L4 ANSWER 5 OF 17 MEDLINE
AN 92263816 MEDLINE
DN 92263816 PubMed ID: 1814050
TI Preliminary studies on subtypes of **respiratory syncytial** virus in China.
AU Du J; Wang Z; Liu C; Wang F; Zhang Y; Zhang S; Chang R; Li H; Duan P
CS Capital Institute of Pediatrics, Beijing.
SO WEI SHENG WU HSUEH PAO [ACTA MICROBIOLOGICA SINICA], (1991 Dec) 31 (6) 488-91.
Journal code: 21610860R. ISSN: 0001-6209.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 199206
ED Entered STN: 19920626
Last Updated on STN: 19920626
Entered Medline: 19920612
AB An analysis of subtypes of 9 **respiratory syncytial** (RS) viruses isolated from Guangzhou and Nanjing areas of china was carried out with eight Sweden RS-subtype specific monoclonal antibodies (MAbs) and 7 internal anti-RS MAbs. All these MAbs directed against respectively the large Glycoprotein (**G**), fusion **protein** (**F**), nucleoprotein (NP), and phosphoprotein (P) components of the prototype Long strain of RS virus. The patterns of the reactions of these MAbs to the nine isolated strains of RS virus were compared with indirect immunofluorescence assay (IFA), alkaline phosphoesterase-anti alkaline phosphoesterase (APAAP) enzyme-linked assay and Western blotting. The antigenic variations were founded among the strains of RS virus, and two subtypes allocated to the subtype **A** and **B** of RS **virus** by using the eight RS-subtype specific MAbs. Seven out of the 9 isolated strains of RS **virus** belonged to the subtype **A**, and two were being to the subtype B. The antigenic diversities were also founded within the same subtype, and the main pronounced difference were observed on the G glycoprotein by using the internal anti-RS MAbs. These findings are potentially important both for vaccine development and for the understanding of clinical and epidemiological characteristics of RS virus.

L4 ANSWER 6 OF 17 MEDLINE
AN 91251232 MEDLINE
DN 91251232 PubMed ID: 1710289
TI Immunodominant T-cell epitope on the F protein of **respiratory syncytial** virus recognized by human lymphocytes.
AU Levely M E; Bannow C A; Smith C W; Nicholas J A
CS Department of Infectious Diseases Research, Upjohn Laboratories, Kalamazoo, Michigan 49007.
SO JOURNAL OF VIROLOGY, (1991 Jul) 65 (7) 3789-96.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199107
ED Entered STN: 19910728
Last Updated on STN: 19960129

Entered Medline: 19910711

AB The lymphocyte proliferative responses to **respiratory syncytial** virus (**RSV**) were evaluated for 10 healthy adult donors and compared with proliferative responses to a **chimeric** glycoprotein (FG glycoprotein) which consists of the extracellular domains of both the **F** and **G** **proteins** of **RSV** and which is produced from a recombinant baculovirus. The lymphocytes of all 10 donors responded to **RSV**, and the proliferative responses to the whole virus were highly correlated with the responses to the FG glycoprotein. These data suggested that one or both of these glycoproteins of **RSV** were major target structures for stimulation of the human lymphocyte proliferative response among virus-specific memory T cells. The lymphocytes of four donors were evaluated further for their proliferative responses to a nested set of overlapping peptides modeled on the extracellular and cytoplasmic domains of the **F protein** of **RSV**. Strikingly, the lymphocytes of all 4 donors responded primarily to a region defined by a single peptide spanning residues 338 to 355, and the lymphocytes of 2 donors responded to an overlapping peptide spanning residues 328 to 342 also, thus defining a region of the F1 subunit within residues 328 to 355 that may circumscribe an immunodominant site for stimulation of human T cells from a variety of individuals. This region of the **F** **protein** is highly conserved among **A** and **B** subgroup **viruses**. As revealed by monoclonal antibody blocking studies, the lymphocytes responding to this antigenic site had characteristics consistent with T helper cells. Similar epitope mapping studies were performed with BALB/c mice immunized with the FG protein in which a relatively hydrophobic peptide spanning residues 51 to 65 within the F2 subunit appeared to be the major T cell recognition determinant. The data are discussed with respect to an antigenic map of the **F** **protein** and the potential construction of a synthetic vaccine for **RSV**.

L4 ANSWER 7 OF 17 MEDLINE
AN 91220716 MEDLINE
DN 91220716 PubMed ID: 2024493
TI Cytotoxic T cell activity against the 22-kDa protein of human **respiratory syncytial virus** (**RSV**) is associated with **a** significant reduction in pulmonary **RSV** replication.
AU Nicholas J A; Rubino K L; Levely M E; Meyer A L; Collins P L
CS Department of Infectious Diseases, Upjohn Laboratories, Kalamazoo, Michigan 49007.
SO VIROLOGY, (1991 Jun) 182 (2) 664-72.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199106
ED Entered STN: 19910623
Last Updated on STN: 19910623
Entered Medline: 19910606

AB Recombinant vaccinia viruses expressing the **RSV F** glycoprotein (Vac-**F**), or **a** previously described **chimeric protein** consisting of the extracellular domains of the **F** and **G** glycoproteins (Vac-FG), or the 22-kDa membrane **protein** (Vac-22 kDa) were evaluated for their ability to protect BALB/c mice against infection by **RSV** subgroup **A** or subgroup **B viruses** and for their ability to induce a humoral immune response or a cytolytic T lymphocyte (CTL)

response. Immunization with Vac-F or Vac-FG fully protected mice against challenge with **RSV** of subgroup **A** or **B** and induced high levels of both humoral and CTL-mediated immunity. Immunization with Vac-22 kDa partially to fully protected mice against challenge with **RSV** of subgroup **A** or **B**, depending on the immunization and challenge conditions, and induced a potent CTL response in the apparent absence of a significant humoral response. These vectors fortuitously allowed us to evaluate the contribution of a protein-specific memory CTL response to subgroup-specific and subgroup-cross-reactive reductions in pulmonary **RSV** replication independently from **a** humoral response. Our data suggest that 22-kDa-specific CTL contribute significantly to the reduction of **RSV** within the lung, but that complete protection also requires a humoral component.

L11 ANSWER 1 OF 7 MEDLINE
AN 2002051326 MEDLINE
DN 21635488 PubMed ID: 11773385
TI Mucosal immunization of rhesus monkeys against **respiratory syncytial virus** subgroups **A** and **B** and human parainfluenza **virus** type 3 by using **a** live cDNA-derived vaccine based on **a** host range-attenuated bovine parainfluenza **virus** type 3 vector backbone.
AU Schmidt Alexander C; Wenzke Daniel R; McAuliffe Josephine M; St Claire Marisa; Elkins William R; Murphy Brian R; Collins Peter L
CS Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.. aschmidt@niaid.nih.gov
NC AI-000030 (NIAID)
AI-000087 (NIAID)
SO JOURNAL OF VIROLOGY, (2002 Feb) 76 (3) 1089-99.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020125
Last Updated on STN: 20020213
Entered Medline: 20020212
AB Reverse genetics was used to develop a two-component, trivalent live attenuated **vaccine** against human parainfluenza virus type 3 (HPIV3) and **respiratory syncytial virus** (**RSV**) subgroups **A** and **B**. The backbone for each of the two components of this vaccine was the attenuated recombinant bovine/human PIV3 (rB/HPIV3), a recombinant BPIV3 in which the bovine HN and F protective antigens are replaced by their HPIV3 counterparts (48). This chimera retains the well-characterized host range attenuation phenotype of BPIV3, which appears to be appropriate for immunization of young infants. The open reading frames (ORFs) for the **G** and **F** major protective antigens of **RSV** subgroup **A** and **B** were each placed under the control of PIV3 transcription signals and inserted individually or in homologous pairs as supernumerary **genes** in the promoter proximal position of rB/HPIV3. The level of replication of rB/HPIV3-**RSV** chimeric viruses in the respiratory tract of rhesus monkeys was similar to that of their parent virus rB/HPIV3, and each of the chimeras induced **a** robust immune response to both **RSV** and HPIV3. **RSV**-neutralizing antibody titers induced by rB/HPIV3-**RSV** chimeric viruses were equivalent to those induced by infection with wild-type **RSV**, and HPIV3-specific antibody responses were similar to, or slightly less than, after infection with the rB/HPIV3 vector itself. This study describes **a** novel **vaccine** strategy against **RSV** in which **vaccine viruses** with **a** common attenuated backbone, specifically rB/HPIV3 derivatives expressing the G and/or F major protective antigens of **RSV** subgroup **A** and of **RSV** subgroup **B**, are used to immunize by the intranasal route against **RSV** and HPIV3, which are the first and second most important viral agents of pediatric respiratory tract disease worldwide.

L11 ANSWER 2 OF 7 MEDLINE
AN 2001409079 MEDLINE
DN 21157740 PubMed ID: 11257359
TI Identification and characterisation of multiple linear B cell protectopes in the **respiratory syncytial** virus G protein.

AU Power U F; Plotnicky-Gilquin H; Goetsch L; Champion T; Beck A; Haeuw J F; Nguyen T N; Bonnefoy J Y; Corvaia N
CS Centre d'Immunologie Pierre Fabre, 74164 Cedex, Saint-Julien-en-Genevois, France.. ultan.power@pierre-fabre.com
SO VACCINE, (2001 Mar 21) 19 (17-19) 2345-51.
Journal code: 8406899. ISSN: 0264-410X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200107
ED Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719
AB **Respiratory syncytial** virus (**RSV**) is an important respiratory pathogen in man, against which no **vaccine** is available. However, recent evidence suggests that antibodies to the **RSV F** and **G proteins** may play an important role in disease prevention. We previously demonstrated that BBG2Na, a subunit **vaccine** candidate including residues 130-230 of the Long strain **G protein**, protects rodents against **RSV** challenge. Using a panel of monoclonal antibodies (MAb) and synthetic peptides, five linear B cell epitopes were identified that mapped to residues 152-163, 165-172, 171-187 (two over-lapping epitopes) and 196-204. Antibody passive transfer and peptide immunisation studies revealed that all were protective. Pepscan analyses of anti-**RSV** -**A** and BBG2Na murine polyclonal sera suggested stronger immunogenicity of some protective epitopes (protectopes) in the context of BBG2Na compared with live virus. However, all the identified murine **B** cell protectopes were conserved in **RSV** seropositive humans. Should these protectopes correspond with protection in humans, BBG2Na may constitute **a** very interesting **vaccine** candidate against **RSV**.

L11 ANSWER 3 OF 7 MEDLINE
AN 2001271406 MEDLINE
DN 21214663 PubMed ID: 11312662
TI Chimeric subgroup **A respiratory syncytial virus** with the glycoproteins substituted by those of subgroup **B** and **RSV** without the M2-2 gene are attenuated in African green monkeys.
AU Cheng X; Zhou H; Tang R S; Munoz M G; Jin H
CS Aviron, 297 N. Bernardo Avenue, Mountain View, CA 94043, USA.
NC 2R44 AI45267-01/02 (NIAID)
SO VIROLOGY, (2001 Apr 25) 283 (1) 59-68.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010521
AB Using the existing reverse genetics system developed for the subgroup **A respiratory syncytial virus** (**RSV**), **a chimeric virus** (designated rA-**G**(**B**)**F**(**B**)) that expresses subgroup B-specific antigens was constructed by replacing the **G** and **F genes** of the A2 strain with those of the 9320 strain of subgroup **B RSV**. rA-**G**(**B**)

F(B) grew well in tissue culture, but it was attenuated in the respiratory tracts of cotton rats and African green monkeys. To further attenuate this **chimeric RSV**, the M2-2 open reading frame was removed from rA-G(B)F(B). rA-G(B)F(B)DeltaM2-2 was highly attenuated in replication in the respiratory tracts of the infected monkeys, but it provided complete protection against wild-type subgroup **B RSV** challenge following two doses of infection. In this study, rA2DeltaM2-2 (**a** recombinant A2 **RSV** that lacks the M2-2 gene) was also evaluated in African green monkeys. The replication of rA2DeltaM2-2 was highly restricted in both the upper and lower respiratory tracts of the infected monkeys and it induced titers of serum anti-**RSV** neutralizing antibody that were slightly lower than those induced by wild-type rA2. When rA2DeltaM2-2-infected monkeys were challenged with wild-type A2 virus, the replication of the challenge virus was reduced by approximately 100-fold in the upper respiratory tract and 45,000-fold in the lower respiratory tracts. rA2DeltaM2-2 and rA-G(B)F(B)DeltaM2-2 could represent **a** bivalent **RSV vaccine** composition for protection against multiple strains from the two **RSV** subgroups.

L11 ANSWER 4 OF 7 MEDLINE
AN 2001222312 MEDLINE
DN 21211609 PubMed ID: 11312329
TI Recombinant bovine/human parainfluenza **virus** type 3 (**B** /HPIV3) expressing the **respiratory syncytial virus** (**RSV**) **G** and **F proteins** can be used to achieve simultaneous mucosal immunization against **RSV** and HPIV3.
AU Schmidt A C; McAuliffe J M; Murphy B R; Collins P L
CS Laboratory of Infectious Disease, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.. aschmidt@niaid.nih.gov
NC AI-000030 (NIAID)
AI-000087 (NIAID)
SO JOURNAL OF VIROLOGY, (2001 May) 75 (10) 4594-603.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524
AB Recombinant bovine/human parainfluenza **virus** type 3 (rB/HPIV3), **a** recombinant bovine PIV3 (rBPIV3) in which the **F** and HN **genes** were replaced with their HPIV3 counterparts, was used to express the major protective antigens of **respiratory syncytial virus** (**RSV**) in order to create **a** bivalent mucosal **vaccine** against **RSV** and HPIV3. The attenuation of rB/HPIV3 is provided by the host range restriction of the BPIV3 backbone in primates. **RSV G** and **F** open reading frames (ORFs) were placed under the control of PIV3 transcription signals and inserted individually into the rB/HPIV3 genome in the promoter-proximal position preceding the nucleocapsid **protein gene**. The recombinant PIV3 expressing the **RSV** G ORF (rB/HPIV3-G1) was not restricted in its replication in vitro, whereas the virus expressing the **RSV** F ORF (rB/HPIV3-F1) was eightfold restricted compared to its rB/HPIV3 parent. Both viruses

replicated efficiently in the respiratory tract of hamsters, and each induced **RSV** serum antibody titers similar to those induced by **RSV** infection and anti-HPIV3 titers similar to those induced by HPIV3 infection. Immunization of hamsters with rB/HPIV3-G1, rB/HPIV3-F1, or **a** combination of both **viruses** resulted in **a** high level of resistance to challenge with **RSV** or HPIV3 28 days later. These results describe a **vaccine** strategy that obviates the technical challenges associated with a live attenuated **RSV vaccine**, providing, against the two leading viral agents of pediatric respiratory tract disease, a bivalent **vaccine** whose attenuation phenotype is based on the extensive host range sequence differences of BPIV3.

L11 ANSWER 5 OF 7 MEDLINE
AN 2000027198 MEDLINE
DN 20027198 PubMed ID: 10559287
TI Replacement of the **F** and **G proteins** of **respiratory syncytial virus** (**RSV**) subgroup **A** with those of subgroup **B** generates **chimeric** live attenuated **RSV** subgroup **B vaccine** candidates.
AU Whitehead S S; Hill M G; Firestone C Y; St Claire M; Elkins W R; Murphy B R; Collins P L
CS Respiratory Viruses Section, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892, USA.. sswhitehead@nih.gov
SO JOURNAL OF VIROLOGY, (1999 Dec) 73 (12) 9773-80.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991220
AB Human **respiratory syncytial** virus (**RSV**) exists as two antigenic subgroups, **A** and B, both of which should be represented in a **vaccine**. The **F** and **G** glycoproteins are the major neutralization and protective antigens, and the **G protein** in particular is highly divergent between the subgroups. The existing system for reverse genetics is based on the A2 strain of **RSV** subgroup **A**, and most efforts to develop **a** live attenuated **RSV vaccine** have focused on strain A2 or other subgroup **A viruses**. In the present study, the development of a live attenuated subgroup B component was expedited by the replacement of the F and G glycoproteins of recombinant A2 virus with their counterparts from the **RSV** subgroup **B** strain B1. This **gene** replacement was initially done for wild-type (wt) recombinant A2 **virus** to create **a** wt AB **chimeric virus** and then for **a** series of A2 derivatives which contain various combinations of A2-derived attenuating mutations located in **genes** other than **F** and **G**. The wt AB virus replicated in cell culture with an efficiency which was comparable to that of the wt A2 and B1 parents. AB viruses containing temperature-sensitive mutations in the A2 background exhibited levels of temperature sensitivity in vitro which were similar to those of A2 viruses bearing the same mutations. In chimpanzees, the replication of the wt AB chimera was intermediate between that of the A2 and B1 wt viruses and was accompanied by moderate rhinorrhea, as previously seen in this species. An AB chimeric virus, rABcp248/404/1030,

which was constructed to contain a mixture of attenuating mutations derived from two different biologically attenuated A2 viruses, was highly attenuated in both the upper and lower respiratory tracts of chimpanzees. This attenuated AB chimeric **virus** was immunogenic and conferred **a** high level of resistance on chimpanzees to challenge with wt AB virus. The rABcp248/404/1030 chimeric **virus** is **a** promising **vaccine** candidate for **RSV** subgroup **B** and will be evaluated next in humans. Furthermore, these results suggest that additional attenuating mutations derived from strain A2 can be inserted into the A2 background of the recombinant chimeric AB virus as necessary to modify the attenuation phenotype in a reasonably predictable manner to achieve an optimal balance between attenuation and immunogenicity in **a virus** bearing the subgroup **B** antigenic determinants.

L11 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:323416 BIOSIS
DN PREV199900323416
TI Identification of multiple protective epitopes (protectopes) in the central conserved domain of a prototype human **respiratory syncytial** virus G protein.
AU Plotnicky-Gilquin, Helene; Goetsch, Liliane; Huss, Thierry; Champion, Thierry; Beck, Alain; Haeuw, Jean-Francois; Ngoc Nguyen, Thien; Bonnefoy, Jean-Yves; Corvaia, Nathalie; Power, Ultan F. (1)
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SO Journal of Virology, (July, 1999) Vol. 73, No. 7, pp. 5637-5645. ISSN: 0022-538X.
DT Article
LA English
SL English
AB A recombinant fusion **protein** (BBG2Na) comprising the central conserved domain of the **respiratory syncytial** virus subgroup **A** (**RSV-A**) (Long) **G** **protein** (residues 130 to 230) and an albumin binding domain of streptococcal **protein G** was shown previously to protect mouse upper (URT) and lower (LRT) respiratory tracts against intranasal **RSV** challenge (U. **F**. Power, H. Plotnicky-Gilquin, T. Huss, A. Robert, M. Trudel, S. Stahl, M. Uhlen, T. N. Nguyen, and H. Binz, Virology 230:155-166, 1997). Panels of monoclonal antibodies (MAbs) and synthetic peptides were generated to facilitate dissection of the structural elements of this domain implicated in protective efficacy. All MAbs recognized native **RSV-A** antigens, and five linear **B**-cell epitopes were identified; these mapped to residues 152 to 163, 165 to 172, 171 to 187 (two overlapping epitopes), and 196 to 204, thereby covering the highly conserved cysteine noose domain. Antibody passive-transfer and peptide immunization studies revealed that all epitopes were implicated in protection of the LRT, but not likely the URT, against **RSV-A** challenge. Pepscan analyses of anti-**RSV-A** and anti-BBG2Na murine polyclonal sera revealed lower-level epitope usage within the central conserved region in the former, suggesting diminished immunogenicity of the implicated epitopes in the context of the whole virus. However, Pepscan analyses of **RSV**-seropositive human sera revealed that all of the murine B-cell protective epitopes (protectopes) that mapped to the central conserved domain were recognized in man. Should these murine protectopes also be implicated in human LRT protection, their clustering around the highly conserved cysteine noose region will have important implications for the development of **RSV vaccines**.

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AN 2000211248 EMBASE
TI CD40 ligand (CD154) enhances the Th1 and antibody responses to **respiratory syncytial** virus in the BALB/c mouse.
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SO Journal of Immunology, (2000) 164/11 (5913-5921).
Refs: 71
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB CD40 ligand (CD40L) is a cell surface costimulatory molecule expressed mainly by activated T cells. CD40L is critically important for T-B cell and T cell-dendritic cell interactions. CD40L expression promotes Th1 cytokine responses to **protein** Ags and is responsible for Ig isotype switching in **B** cells. **Respiratory syncytial** virus (**RSV**) is an important pathogen of young children and the elderly, which causes bronchiolitis and pneumonia. Studies of mice infected with **RSV** suggest that **a** Th2 cytokine response may be responsible for enhanced pulmonary disease. To investigate the effect CD40L has on **RSV** immunity, mice were infected simultaneously with **RSV** and either an empty control adenovirus vector or one expressing CD40L or were coimmunized with plasmid DNA vectors expressing CD40L and **RSV F** and/or **G proteins** and subsequently challenged with **RSV**. The kinetics of the intracellular and secreted cytokine responses, the cytotoxic T lymphocyte precursor frequency, NO levels in lung lavage, rates of virus clearance, and anti-**RSV** Ab titers were determined. These studies show that coincident expression of CD40L enhances the Th1 (IL-2 and IFN-.gamma.) cytokine responses, increases the expression of TNF-.alpha. and NO, accelerates virus clearance, and increases the anti-**F** and anti-**G** Ab responses. These data suggest that CD40L may have the adjuvant properties needed to optimize the safety and efficacy of **RSV vaccines**.